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09/827,289	04/05/2001	Patricio Abarzua	469290-55	5725

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EXAMINER	
FREDMAN, JEFFREY NORMAN	
ART UNIT	PAPER NUMBER
1637	8

DATE MAILED: 07/29/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/827,289	Applicant(s) ABARZUA, PATRICIO	
	Examiner Jeffrey Fredman	Art Unit 1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 June 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-30* is/are pending in the application.

4a) Of the above claim(s) *16,17 and 30* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-14 and 18-29* is/are rejected.

7)☒ Claim(s) *15* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I in Paper No. 7 is acknowledged. The traversal is on the ground(s) that there is no burden in searching for the kit. This is not found persuasive for several reasons. First, the separate classification is prima facie evidence of burden which has not been rebutted. Second, the argument that the instructions impose the same method requirements onto the product of Group II as are found in the method of Group I is incorrect as a matter of law. Instructions do not carry patentable weight, as noted by MPEP 2111.02. The CAFC in In re Gulack notes "Where the printed matter is not functionally related to the substrate, the printed matter will not distinguish the invention from the prior art in terms of patentability." In re Gulack, 703 F.2d 1381, 1385, 217 U.S.P.Q. (BNA) 401, 404 (Fed. Cir. 1983). Here, the printed matter is not functionally related to the product in any way.

Consequently, claims 16, 17 and 30 are withdrawn from consideration as drawn to non-elected Groups.

The requirement is still deemed proper and is therefore made FINAL.

Claim Rejections - 35 USC § 102

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. Claims 1 and 9 are rejected under 35 U.S.C. 102(b) as being anticipated by Eyal et al (U.S. Patent 5,710,028).

Chee teaches a method of detecting single nucleotide polymorphisms (abstract) comprising:

(a) contacting an allele specific oligonucleotide primer with a target polynucleotide, wherein the target polynucleotide has a first portion which is complementary to a second portion on the allele specific oligonucleotide primer under conditions which permit hybridization between the two portions (column 16, lines 25-64),

(b) contacting the complex of primer and target nucleic acids with an exonuclease deficient DNA polymerase which extends the primer (see column 16, line 49 to column 17, line 18) including the use of Klenow, Sequenase, T5 DNA polymerase and Phi29 DNA polymerase among others (column 17, lines 10-12),

(c) detecting the extended primer (column 17, lines 36-43).

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation

under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 1-14 and 18-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Eyal et al (U.S. Patent 5,710,028) in view of Chee et al (U.S. Patent 6,355,431).

Eyal teaches a method of detecting single nucleotide polymorphisms (abstract) comprising:

(a) contacting an allele specific oligonucleotide primer with a target polynucleotide, wherein the target polynucleotide has a first portion which is complementary to a second portion on the allele specific oligonucleotide primer under conditions which permit hybridization between the two portions (abstract and column 11, lines 29-38),

(b) contacting the complex of primer and target nucleic acids with an DNA polymerase which extends the primer (see column 11, lines 39-51),

(c) detecting the extended primer by detecting the presence of another oligonucleotide on a solid support which is hybridized to the extended primer (column 7, lines 27-67).

Eyal teaches detection of genomic DNA (see column 2, lines 1-3) as well as non-human DNA such as that in pathogens like HIV (see column 15-20).

Eyal teaches diagnosis of a disease in humans by determining the presence of a mutated gene sequence including cystic fibrosis (see column 24, example 1 and column 26, example 4). Eyal further teaches diagnosis of cancer by detection of point mutations (see column 1, lines 63-65).

Eyal does not teach the use of an exonuclease deficient polymerase nor does Eyal teach detection using rolling circle amplification.

Chee teaches a method of detecting single nucleotide polymorphisms (abstract) comprising:

(a) contacting an allele specific oligonucleotide primer with a target polynucleotide, wherein the target polynucleotide has a first portion which is complementary to a second portion on the allele specific oligonucleotide primer under conditions which permit hybridization between the two portions (column 16, lines 25-64),

(b) contacting the complex of primer and target nucleic acids with an exonuclease deficient DNA polymerase which extends the primer (see column 20 and column 16, line 49 to column 17, line 18) including the use of Klenow, Sequenase, T5 DNA polymerase and Phi29 DNA polymerase among others (column 17, lines 10-12),

(c) detecting the extended primer (column 17, lines 36-43).

Chee further teaches detection of the single base extended product using rolling circle amplification with an additional primer that forms a circle (see columns 19-22).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to modify the method of Eyal, which is a method in which a single base extension is detected by hybridization to a probe with a label, by using

the method of Chee who teaches detection of single base extension using a probe with a label where the label enables rolling circle amplification, since the rolling circle amplification of Chee will very significantly increase the signal, making the method of Eyal more sensitive and more accurate. As Chee notes,

> "The RCA as described herein finds use in allowing highly specific and highly sensitive detection of nucleic acid target sequences. In particular, the method finds use in improving the multiplexing ability of DNA arrays and eliminating costly sample or target preparation. As an example, a substantial savings in cost can be realized by directly analyzing genomic DNA on an array, rather than employing an intermediate PCR amplification step. The method finds use in examining genomic DNA and other samples including mRNA. In addition the RCA finds use in allowing rolling circle amplification products to be easily detected by hybridization to probes in a solid-phase format (e.g. an array of beads). An additional advantage of the RCA is that it provides the capability of multiplex analysis so that large numbers of sequences can be analyzed in parallel. By combining the sensitivity of RCA and parallel detection on arrays, many sequences can be analyzed directly from genomic DNA. (column 22, lines 42-59)".

Thus, an ordinary practitioner would have been motivated to use RCA as a detectable label in the method of Eyal since RCA saves money, permits multiplexing, increases sensitivity and permits direct detection of genomic DNA.

7. Claims 1-14 and 18-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Eyal et al (U.S. Patent 5,710,028) in view of Chee et al (U.S. Patent

6,355,431) and further in view of Ishikawa et al (Human Immunology (1995) 42:315-318).

Eyal in view of Chee teach the limitations of claims 1-14 and 18-25 as discussed above. Eyal in view of Chee do not teach the use of primers with mismatches near the 3' termini.

Ishikawa teaches that putting mismatches in primers near the 3' termini increases the specificity of amplification (abstract and page 316, column 2).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to modify the method of Eyal in view of Chee for single base amplification using primers to use primers which have been modified to improve specificity as taught by Ishikawa since Ishikawa states "the introduction of an additional one-base mismatch is a simple and useful way to improve the specificity (page 316, column 2)". An ordinary practitioner would have been motivated to modify the primers of Eyal in view of Chee by creating mismatches near the 3' end in order to improve the specificity of the single base extension reaction, thereby improving the quality of the assay and reducing the number of false negative and false positives which would otherwise occur.

Allowable Subject Matter

8. The elected Restriction subgroup, SEQ ID NO: 13, is novel and unobvious over the cited prior art. While the targeting region to cystic fibrosis is known, the particular sequence with the particular number of T residues attached is not taught by the prior art and is not obvious. Currently claim 15 is objected to as dependent from a rejected

claim but if it was limited to the elected subgroup and rewritten in independent form, the claims would be allowable.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey Fredman whose telephone number is 703-308-6568. The examiner can normally be reached on 6:30-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 703-308-1119. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Jeffrey Fredman
Primary Examiner
Art Unit 1637

July 23, 2002